S1 Ordinary differential equations (ODEs) of in AA metabolic pathway

Based on the rules in Materials and Methods, we have constructed ODEs for all species in the AA metabolic pathway, as follows:

1) $$\frac{d[AA]}{dt}=\frac{K_{cat,PLA2}\times[PLA_2][PL]}{k_{m,PLA2}\times\left(1+\frac{[AA]}{ki}\right)+[PL]}-\frac{K_{cat,COX2}\times[COX2][AA]}{k_{m,COX2}\times\left(1+\frac{[PGH_2]}{ki}\right)+[AA]}-\frac{K_{cat,12-LO}\times[12-LO][AA]}{k_{m,12-LO}\times\left(1+\frac{[12-HpETE]}{ki}\right)+[AA]}$$

$$-\frac{K_{cat,5-LO}\times[5-LO][AA]}{k_{m,5-LO}\times\left(1+\frac{[AA]}{k_{AA\to5-LO}}+\frac{[15-HETE]}{k_{15-HETE\to5-LO}}+\frac{[5-HETE]}{k_{5-HETE\to5-LO}}+\frac{[LTA_4]}{k_{LTA_4\to5-LO}}+\frac{[5-HpETE]}{ki}+\frac{[JH-2]}{k_{inht5LO}}\right)+[AA]}$$

$$-\frac{K_{cat,12-LO}\times[12-LO][AA]}{k_{m,12-LO}\times\left(1+\frac{[12-HpETE]}{ki}\right)+[AA]}-\frac{K_{cat,15-LO}\times[15-LO][AA]}{k_{m,15-LO}\times\left(1+\frac{[15-HpETE]}{ki}+\frac{[JH-2]}{k_{inht15LO}}\right)+[AA]}$$

$$-kd_{AA}\times[AA]$$

2) $$\frac{d[15-HpETE]}{dt}=\frac{K_{cat,15-LO}\times[15-LO][AA]}{k_{m,15-LO}\times(1+\frac{[15-HpETE]}{ki}+\frac{[JH-2]}{k_{inht15LO}})+[AA]}-\frac{K_{cat,PHGPx}\times[PHGPx][15-HpETE]}{k_{m,PHGPx}\times(1+\frac{[15-HETE]}{ki})+[15-HpETE]}$$

3) $$\frac{d[15-HETE]}{dt}=\frac{K_{cat,PHGPx}\times[PHGPx][15-HpETE]}{k_{m,PHGPx}\times(1+\frac{[15-HETE]}{ki})+[15-HpETE]}-kd_{15-HETE}\times[15-HETE]$$

4) $$\frac{d[12-HpETE]}{dt}=\frac{K_{cat,12-LO}\times[12-LO][AA]}{k_{m,12-LO}\times(1+\frac{[12-HpETE]}{ki})+[AA]}-\frac{K_{cat,PHGPx}\times[PHGPx][12-HpETE]}{k_{m,PHGPx}\times(1+\frac{[12-HETE]}{ki})+[12-HpETE]}$$

5) $$\frac{d[12-HETE]}{dt}=\frac{K_{cat,PHGPx}\times[PHGPx][12-HpETE]}{k_{m,PHGPx}\times(1+\frac{[12-HETE]}{ki})+[12-HpETE]}-kd_{12-HETE}\times[12-HETE]$$

6) $$\frac{d[5-HpETE]}{dt}=$$

$$\frac{K_{cat,5-LO}\times[5-LO][AA]}{k_{m,5-LO}\times\left(1+\frac{[AA]}{k_{AA\to5-LO}}+\frac{[15-HETE]}{k_{15-HETE\to5-LO}}+\frac{[5-HETE]}{k_{5-HETE\to5-LO}}+\frac{[LTA_4]}{k_{LTA_4\to5-LO}}+\frac{[5-HpETE]}{ki}+\frac{[JH-2]}{k_{inht5LO}}\right)+[AA]}$$

$$-\frac{K_{cat,5-LO}\times[5-LO][5-HpETE]}{k_{m,5-LO}\times\left(1+\frac{[AA]}{k_{AA\to5-LO}}+\frac{[15-HETE]}{k_{15-HETE\to5-LO}}+\frac{[5-HETE]}{k_{5-HETE\to5-LO}}+\frac{[LTA_4]}{k_{LTA_4\to5-LO}}+\frac{[5-HpETE]}{ki}+\frac{[JH-2]}{k_{inht5LO}}\right)+[5-HpETE]}$$

$$-\frac{K_{cat,PHGPx}\times[PHGPx][5-HpETE]}{k_{m,PHGPx}\times(1+\frac{[5-HETE]}{ki})+[5-HpETE]}$$

7) $$\frac{d[5-HETE]}{dt}=\frac{K_{cat,PHGPx}\times[PHGPx][5-HpETE]}{k_{m,PHGPx}\times(1+\frac{[5-HETE]}{ki})+[5-HpETE]}-kd_{5-HETE}\times[5-HETE]$$

8) $$\frac{d[LTA4]}{dt}=$$

$$\frac{K_{cat,5-LO}\times[5-LO][5-HpETE]}{k_{m,5-LO}\times\left(1+\frac{[AA]}{k_{AA\to5-LO}}+\frac{[15-HETE]}{k_{15-HETE\to5-LO}}+\frac{[5-HETE]}{k_{5-HETE\to5-LO}}+\frac{[LTA_4]}{k_{LTA_4\to5-LO}}+\frac{[5-HpETE]}{ki}+\frac{[JH-2]}{k_{inht5LO}}\right)+[5-HpETE]}$$

$$-\frac{K_{cat,LTA4H}\times[LTA4H][LTA_4]}{k_{m,LTA4H}\times(1+\frac{[LTA_4]}{k_{LTA4\to LTA4H}}+\frac{[LTB_4]}{ki})+[LTA_4]}-\frac{K_{cat,LTC4S}\times[LTC4S][LTA_4]}{k_{m,LTC4S}\times(1+\frac{[LTA_4]}{k_{LTA4\to LTC4S}}+\frac{[LTC_4]}{ki})+[LTA_4]}$$

9) $$\frac{d[LTB_4]}{dt}=-\frac{K_{cat,LTA4H}\times[LTA4H][LTA_4]}{k_{m,LTA4H}\times(1+\frac{[LTA_4]}{k_{LTA4\to LTA4H}}+\frac{[LTB_4]}{ki})+[LTA_4]}-kd_{LTB4}\times LTB_4$$

10) $$\frac{d[LTC_4]}{dt}=-\frac{K_{cat,LTC4S}\times[LTC4S][LTA_4]}{k_{m,LTC4S}\times(1+\frac{[LTA_4]}{k_{LTA4\to LTC4S}}+\frac{[LTC_4]}{ki})+[LTA_4]}-kd_{LTC4}\times LTC_4$$

11) $$\frac{d[PGH_2]}{dt}=\frac{K_{cat,COX2}\times[COX2][AA]}{k_{m,COX2}\times(1+\frac{[PGH_2]}{ki})+[AA]}-\frac{K_{cat,PGDS}\times[PGDS][PGH_2]}{k_{m,PGDS}\times\left(1+\frac{[PGD_2]}{ki}\right)+[PGH_2]}$$

$$-\frac{K_{cat,PGFS}\times[PGFS][PGH_2]}{k_{m,PGFS}\times\left(1+\frac{[PGF_{2\alpha}]}{ki}\right)+[PGH_2]}-\frac{K_{cat,TXAS}\times[TXAS][PGH_2]}{k_{m,TXAS}\times\left(1+\frac{[PGH_2]}{k_{PGH2\to TXAS}}+\frac{[TXA_2]}{ki}\right)+[PGH_2]}$$

$$-\frac{K_{cat,PGES}\times[PGES][PGH_2]}{k_{m,PGES}\times\left(1+\frac{[AA]}{k_{AA\to PGES}}+\frac{[LTC_4]}{k_{LTC4\to PGES}}+\frac{[PGE_2]}{ki}\right)+[PGH_2]}-kd_{PGH2}\times PGH_2$$

12) $$\frac{d[PGE_2]}{dt} = \frac{K_{cat,PGES} \times [PGES][PGH_2]}{k_{m,PGES} \times \left(1 + \frac{[AA]}{k_{AA \to PGES}} + \frac{[LTC_4]}{k_{LTC4 \to PGES}} + \frac{[PGE_2]}{ki}\right) + [PGH_2]} - kd_{PGE2} \times PGE_2$$

13) $$\frac{d[PGD_2]}{dt} = \frac{K_{cat,PGDS} \times [PGDS][PGH_2]}{k_{m,PGDS} \times \left(1 + \frac{[PGD_2]}{ki}\right) + [PGH_2]} - kd_{PGD2} \times PGD_2$$

14) $$\frac{d[PGF_{2\alpha}]}{dt} = \frac{K_{cat,PGFS} \times [PGFS][PGH_2]}{k_{m,PGFS} \times \left(1 + \frac{[PGF_{2\alpha}]}{ki}\right) + [PGH_2]} - kd_{PGF2\alpha} \times PGF_{2\alpha}$$

15) $$\frac{d[TXA_2]}{dt} = \frac{K_{cat,TXAS} \times [TXAS][PGH_2]}{k_{m,TXAS} \times \left(1 + \frac{[PGH_2]}{k_{PGH2 \to TXAS}} + \frac{[TXA_2]}{ki}\right) + [PGH_2]} - kd_{TXA2} \times TXA_2$$

16) $$\frac{d[TXB_2]}{dt} = kd_{TXA2} \times TXA_2 - kd_{TXB2} \times TXB_2$$

17) $$\frac{d[PLA_2]}{dt} = 0$$

18) $$\frac{d[15-LO]}{dt} = -k_{inht15LO} \times [JH-2] \times [15-LO]$$

19) $$\frac{d[PHGPx]}{dt} = 0$$

20) $$\frac{d[12-LO]}{dt} = 0$$

21) $$\frac{d[5-LO]}{dt} = -k_{inht5LO} \times [JH-2] \times [5-LO]$$

22) $$\frac{d[LTA4H]}{dt} = 0$$

23) $$\frac{d[LTC4S]}{dt} = 0$$

24) $$\frac{d[COX2]}{dt} = 0$$

25) $$\frac{d[PGES]}{dt} = 0$$

26) $$\frac{d[PGDS]}{dt}=0$$

27) $$\frac{d[PGFS]}{dt}=0$$

28) $$\frac{d[TXAS]}{dt}=0$$

29) $$\frac{d[JH-2]}{dt}=-k_{on5LO}\times[JH-2]\times[5-LO]+k_{on5LO}\times k_{inht5LO}\times[comp5LO]$$
$$-k_{on15LO}\times[JH-2]\times[15-LO]+k_{on15LO}\times k_{inht15LO}\times([itotal]-[comp5LO]-[JH-2])$$

30) $$\frac{d[comp5LO]}{dt}=k_{on5LO}\times[JH-2]\times[5-LO]-k_{on5LO}\times k_{inht5LO}\times[comp5LO]$$

*JH-2 is the code name of HOEC, comp5LO is the complex of HOEC and 5-LO.

S2.1 Initial values of parameters

The initial values of the metabolites which have been measured were taken from the experimental values, and the others were given a default value directly. The initial value of the kinetic parameters of the enzyme was queried from the BRENDA [1] database, as shown in Table S1. Since no query results were available of 5-LOX and PHGPx, the initial values of them were based on the fitting values of the AA metabolic pathway model of human neutrophils established by Lai Luhua et al. In addition, we have also collected and collated the feedback pathways included in the AA pathway, as shown in Table S2.

Table S1 Enzyme kinetic parameters involved in AA metabolic pathway (experimental data)

Enzymes	K_{cat} (min^{-1})	K_m (μM)	K_{cat}/K_m	Data sources
PLA_2 [2]	35	8.24	4.24	Rattus norvegicus
COX-2 [3]	1620	5.14	315.18	Mus musculus, (N580A COX2)
PGDS [4]	124.3	0.8	155.38	Mus musculus, (L-PGDS)
PGES [5]	3000	160	18.75	Homo sapiens
PGFS [6]	14.8	6.9	2.14	Mus musculus
TXAS [7]	14.79	10	1.48	Homo sapiens
5-LOX	/	/	/	/

LTA4H [8]	51	6	8.50	Homo sapiens
LTC4S [9]	4860	36	135.00	Mus musculus
12-LOX [10]	693.72	8.2	84.60	Oryctolagus cuniculus
15-LOX [11]	595.8	3.7	161.03	Homo sapiens
PHGPx	/	/	/	/

Table S2 Feedback parameters involved in AA metabolic pathway (experimental data)

Feedbacks	Value (μM)	Type
AA→PGES [12]	0.3	IC_{50}
15-HETE→5-LOX [13]	4	IC_{50}
5-HETE→5-LOX [14]	6.3	K_i
5-HpETE→5-LOX [14]	0.5	K_i
PGH_2→TXAS [15]	18	K_i
LTA_4→LTA4H [16]	3.7 (2°C)	K_i *(irreversible)*
LTC_4→PGES [17]	1.2	IC_{50}
LTA_4→5-LOX [18]	2	K_i *(irreversible)*
LTA_4→LTC4S [19]	2.3	K_i
AA→5-LOX [20]	13.7	K_i

S2.2 Fitted value of parameter

We used the parameter fitting tool of MATLAB and manual debug to obtain a set of parameters to reproduce the changes of metabolites with time in AA pathway after stimulated. The fitted enzyme kinetic parameters, non-enzymatic catalysis and the initial concentrations of enzymes and small molecules in the model are shown in the Table S3-S5

Table S3 Enzyme kenetic parameters involved in AA metabolic network (fitting data)

Enzymes	K_{cat} (1/min)	K_m (μM)
PLA_2	35	8.24
COX-2	5620	5.14
PGDS	224.3	0.8

PGES	5760	122.252
PGFS	14.8	6.9
TXAS	27.79	9.991
5-LOX	2436.16	12.8
LTA4H	343	0.6
LTC4S	4860	3.6
12-LOX	693.7	8.2
15-LOX	595.8	4.7
PHGPx	500	70

Table S4 Non-enzyme kinetic parameters involved in AA metabolic network (fitting data)

Parameter	Reaction	Rate of decay (1/min)
kd1	AA→	0.74
kd2	LTB_4→	0.104
kd3	LTC_4→	0.258
kd4	PGE_2→	0.094
kd5	PGD_2→	0.08
kd6	$PGF_{2\alpha}$→	0.11
kd7	TXA_2→	5.38
kd8	TXB_2→	0.049
kd9	PGH_2→	0.019
kd10	5-HETE→	0.0099
kd11	15-HETE→	0.00045
kd12	12-HETE→	0.0048

Table S5 Initial concentrations of enzymes and molecules involved in AA metabolic network (fitting data)

Parameter	Initial concentration (nM)	Parameter	Initial concentration (nM)
PGH2 (0)	0.00075	**TXB_2 (0)**	0.857
AA (0)	334.102	**PLA_2 (0)**	350.3
15-HETE (0)	3.772	**15-LOX (0)**	1053.23
5-HETE (0)	0.3	**5-LOX (0)**	560.93

12-HETE (0)	0.13	**12-LOX (0)**	65.64
15-HpETE (0)	0.000128	**LTA4H (0)**	1230.8
5-HpETE (0)	0.00078	**LTC4S (0)**	58.52
12-HpETE (0)	0.00019	**PHGPx (0)**	539.78
LTA_4 (0)	0.000176	**COX (0)**	2700.63
LTB_4 (0)	0.1273	**PGDS (0)**	6708.96
LTC_4 (0)	0.336	**PGES (0)**	203.97
PGD_2 (0)	113.316	**PGFS (0)**	378.23
PGE_2 (0)	13.134	**TXAS (0)**	36.72
$PGF_{2\alpha}$ (0)	3.56	**HOEC (0)**	0
TXA_2 (0)	0.000241	**COMP5LO (0)**	0

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